International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 07, July 2024,
https://doi.org/10.23958/ijirms/vol09-i07/1921

Original article

Influence of Age, Sex and Anthropometry on Inspiratory Flow Rates of Patients with Chronic Obstructive Pulmonary Disease

Adebola Oluwabusayo Adetiloye [1,2], Alexander Agada Akor [3], Olayemi Fehintola Awopeju [1], Olufemi Olanisun Adewole [1], Olurotimi John Badero [4], Gregory Efosa Erhabor [1]

[1]Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.
[2]New York City Health and Hospitals/Harlem Hospital Center, NYC, USA.
[3]University of Abuja Teaching Hospital, Gwagwalada, Nigeria.
[4]American College of Cardiology, Washington DC, USA.

*Corresponding Author: Adebola Oluwabusayo Adetiloye; *boladocadetiloye@yahoo.com*; *adetiloa@nychhc.org*

Received 23 June 2024; Accepted 08 July 2024; Published 10 July 2024

Abstract

Introduction: Chronic Obstructive Pulmonary Disease (COPD) affects millions of people with increasing global prevalence, morbidity and mortality. Inhaled medications are central to the management of COPD. Therefore, understanding the minimum Peak Inspiratory Flow (PIF) requirements for inhaler devices is vital for optimal drug delivery. This study assessed PIF in patients with COPD compared with controls and, the influence of age, sex and anthropometric measurements on PIF. ***Methodology:*** A total of 150 subjects (75 patients with stable COPD, and 75 controls) participated in the study. Demographic and anthropometric data were collected from the study participants. Peak inspiratory flow was assessed using the In-check peak flow meter. Lung function was assessed by spirometry. In all the statistical tests, a p value of <0.05 was considered significant. ***Results:*** The control group had higher PIF than COPD group. All of the COPD patients had clinically effective PIF for Clickhaler, Diskus, Easibreathe, and pMDI. Majority of the COPD patients had clinically effective PIF for Turbohaler, and Autohaler. The mean PIF of male patients with COPD was significantly greater than that of females for Turbohaler. For the COPD group, there was a significant negative correlation between PIF and age for Diskus, Autohaler and Easibreathe. Significant positive correlation was also noted between PIF and weight for turbohaler, autohaler and easibreathe. ***Conclusion:*** Majority of COPD patients utilizing dry powder inhalers (DPIs) are able to generate effective PIF. Increasing age, female gender, low body weight and low BMI may contribute to low PIF.

Keywords: ***Chronic Obstructive Pulmonary Disease (COPD), Peak Inspiratory Flow (PIF), Dry Powder Inhaler (DPI), pMDI (pressurized Metered Dose Inhaler)***

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive obstructive respiratory disorder, impacting millions worldwide with escalating global prevalence, morbidity, and mortality [1]. It ranks as the third leading cause of death globally, exerting a detrimental effect on the quality of life for those affected [2,3]. COPD is characterized by persistent respiratory symptoms (dyspnea, cough, sputum production) and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development [4].

Inhaled bronchodilators and inhaled corticosteroids (ICS) are crucial in the management of COPD to control symptoms, enhance quality of life, and avoid exacerbations and costly hospitalization [5]. The choice of inhaler device is critical to ensure optimal drug delivery to the airways. All inhaler devices require an energy source to generate fine drug particles and deliver them into the airways through the inspiratory airflow [6]. Pressurized metered dose inhalers (pMDI's) and nebulizers use propellant or pressurized air as energy source to generate the fine particle which can be taken up by the inspiratory airflow for further transport into the lungs while the dry powder inhalers (DPI's) use the patients generated peak inspiratory flow (PIF) as energy source. Peak inspiratory flow is the maximal airflow generated during a forced inspiratory maneuver [7]. After activation of a DPI device, the patient's PIF controls the disintegration of the powder formulation, followed by the delivery and deposition of the fine particles into the respiratory tract. Optimal" PIF refers to the inspiratory flow necessary for producing a high fine-particle fraction, facilitating the delivery of an adequate portion of the total drug throughout the lungs. A "suboptimal" PIF may lead to inadequate drug-carrier disaggregation and insufficient drug deposition deep in the airways, potentially resulting in medication inefficacy and side effects due to oropharyngeal deposition [8]. Therefore, the PIF flow has to be high enough for optimal DPI performance [9].

DPI devices are manufactured with varying internal resistance. In-vitro test have shown that for adequate dose delivery of medication into the airway, a minimum PIF of 30L/min and above through the inhaler is required. Although, optimal" PIFs, varying from 30 to 65 L/min, have been documented for different DPIs, contingent on the distinctive internal resistance of each DPI, PIF of >60L/min are generally believed to be optimal flow for most devices [10,11]. In ideal situations, the choice for the most appropriate DPI in inhalational therapy should, therefore, depend on the objective measurement of peak inspiratory flow against a certain resistance. Unfortunately, some patients with COPD may have problem generating adequate PIF for optimal DPI use, especially during acute exacerbation [12]. Only a few studies have assessed the ability of patients with COPD to use various inhaler devices and, the effects of age, sex and anthropometric measurements on PIF.

Methodology

Study population

The study is a cross-sectional analysis of 75 stable COPD patients carried out at the Obafemi Awolowo University Teaching Hospital Complex, OAUTHC, Ile-Ife, Osun State, Nigeria. Sample size was determined by the formula for estimating a single proportion at a specified precision.

Inclusion Criteria

- Clinically stable COPD patients
- Diagnosis of COPD is according to GOLD guidelines with the percentage of forced expiratory volume in one second (FEV1) less than 80% predicted and ratio of forced expiratory volume in one second to forced vital capacity (FEV1/FVC) less 70%. No evidence of significant reversibility (reversibility is define by > 12% post bronchodilator testing improvement on FEV1 or change of more than 200ml with administration of short acting β2 agonist in a dose of 400µg of salbutamol).
- Clinically stable is defined by; no change in medication dosage or frequency of administration and no exacerbation or hospital admission in the preceding twelve weeks.

Exclusion criteria

- Patients with active disease like tuberculosis or bronchiectasis.
- Presence of co-morbid medical conditions like neuromuscular diseases, which could affect inhalation through inhaler devices

Controls

- Controls comprise of 75 age-matched subjects who are lifetime never smokers, with no reported disease or symptoms of respiratory diseases and with normal lung function parameters recruited from the general outpatient clinic.

Pulmonary function measurements

Pulmonary function variables were measured according to the American Thoracic Society guidelines for pulmonary function testing and the results were expressed as a percentage of the predicted normal values [13]. Test was performed using a standardized spirometer Spiro-lab II (MIR series) manufactured by SDI diagnostic U.S.A COPD patients were asked to withhold long-acting b2-agonist use for 12 h prior to the lung function tests. During the test, the subjects stay in correct posture by having them sit down on a comfortable chair with head slightly elevated. With the breathing tube inserted into their mouth, the patient seals his or her lips around the mouthpiece ensuring the tongue does not occlude it. The subjects first inhaled rapidly and completely from functional residual capacity, (FRC) and then exhaled maximally to expel all air in the lungs while maintaining an upright posture. Throughout the manoeuvre, enthusiastic coaching of the subject using appropriate body language and phrases, such as "keep going" were employed. After three acceptable spirograms, it was determined if the two largest values of FVC were within 0.150 L of each other and if the two largest values of FEV1 were within 0.150 L of each other. If both of these criteria are met, the test session was concluded [14].

Peak inspiratory flow measurements

PIF measurement was performed with the In-Check Inhaler Assessment Kit (manufactured by Clement Clarke International Ltd, Harlow, UK), a portable hand-held Inspiratory flow meter that provides an assessment of the speed of inhalation. This device compares PIF rates over different DPIs commonly used for the administration of inhaled pharmacotherapeutics for COPD. As PIF is a potential indicator for effective DPI use; PIFs exceeding 60 L/min are considered optimal for the majority of devices, whereas PIFs below 30 L/min are acknowledged as inadequate for producing any effect. The calibration of the in-check flow meter was by ATS pulmonary waveform generator at body temperature and ambient pressure saturated with water vapour. Intra-instrument repeatability was, 5% or 0.150 L. s-1 (5 L.min-1), whichever was the greater. Inter-device reproducibility was, 10% or 0.300 L. s-1 (10 L.min-1), whichever was greater. The patients were instructed to exhale gently (to functional residual capacity) and then to inhale as fast and long as possible through the flow meter with their lips sealed around the mouthpiece. By checking the position of the cursor against the calibrated scale, the flow rate achieved was noted. The highest value from three consecutive PIF measurements, taken after practicing the inhalation manoeuvre, was recorded. [9].

Statistical analysis

Data was analysed using statistical package for social science (SPSS 26) statistical software. Descriptive statistics of frequencies and percentages were used to describe the socio-demographic characteristics of the respondents and their PIF across the varying internal resistance of DPIs and pMDI. To explore potential associations among the variables, Pearson correlation coefficients, one-way ANOVA, and independent t-tests were conducted. In all the statistical tests, a p value of <0.05 was considered significant.

Results

Demographic and anthropometric characteristics of the study participants

Descriptive statistics of frequencies and percentages were used to analyse the demographic characteristics of the respondents. A total of 150 subjects (75 patients with COPD, and 75 apparently healthy subjects) participated in the study. Majority of the subjects in the COPD group (58.7%) and the control group (57.3%) were males. Majority (52.0%) of the subjects in the COPD group were within the age range of 70-79 years. Similarly, majority (53.3%) of the subjects in the control group were within the age range of 70-79 years. Other baseline characteristics are shown in Table 1. More than half of patients with COPD (55%) had normal BMI while 23% were underweight. Approximately 22% of COPD patients were overweight or obese (Figure 1).

Table 1: Baseline characteristics of COPD patients and the control group

Variable	Mean ± SD	Mean ± SD	t-value	p-value
	Patients	**Control**		
Age	72.48 ± 8.01	70.69 ± 5.82	1.56	0.121
BMI	21.96 ± 4.56	25.45 ± 4.58	-4.69	0.000*
Height	1.62 ± 0.07	1.64 ± 0.06	-1.08	0.281
Weight	58.55 ± 10.88	67.73 ± 11.07	-5.12	0.000*
FEV1%	48.08 ± 18.33	107.97 ± 9.81	-24.95	0.000*
FVC%	69.15 ± 18.09	102.77 ± 7.82	-14.78	0.000*

BMI: Body Mass Index

FEV1: Forced Expiratory volume in 1 seconds

FVC: Forced vital capacity

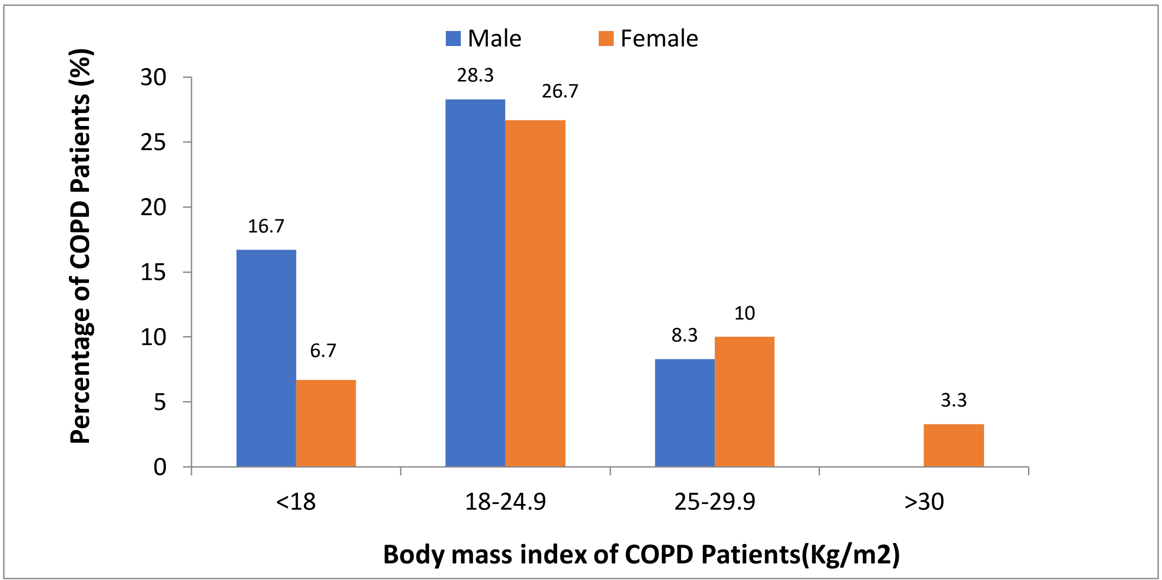

Figure 1: Body Mass Index (BMI) of COPD patients

Peak inspiratory flow rate (PIF) in patients with COPD across simulated internal resistance of DPI and pMDI devices compared with healthy control subjects.

Independent t-test was used to determine the difference between the means of PIF (across varying internal resistance of DPI and pMDI devices) of patients with COPD compared with control group. There was an observed trend of a higher mean PIF in the control group compared with COPD patients across the simulated internal resistance of the DPIs and the pMDI. For Clickhaler and pMDI, the mean PIF of the control group was significantly higher than that of the patients. (Figure 2).

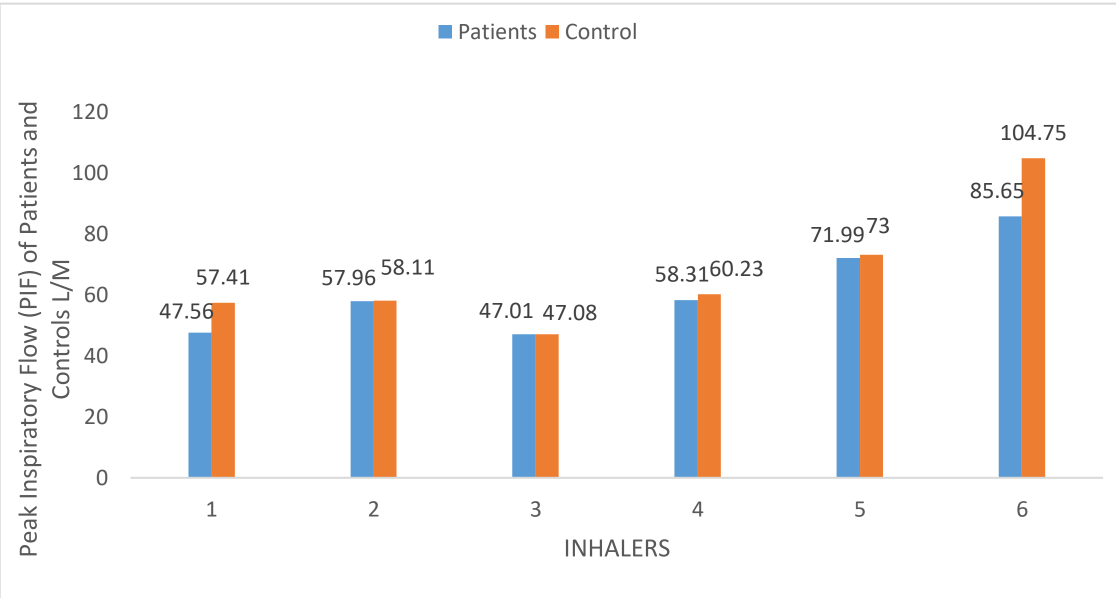

Fig2: Peak inspiratory flow (PIF) of patients and control across Dry powder inhalers (DPIs) and pressurized metered dose inhaler (pMDI)

Key: 1- Clickhaler (p 0.000*), 2- Diskus (p 0.953), 3- Turbohaler (p 0.970), 4- Autohaler (p 0.470), 5- Easibreathe (p 0.748), 6- pMDI (p 0.000*)

Optimal versus Suboptimal PIF in the COPD and Control group

Descriptive statistics of frequencies and percentages were used to analyse the PIF categories (optimal vs suboptimal) of patients and controls across the simulated internal resistance of DPIs and pMDI. All of the COPD patients had clinically effective PIF on Clickhaler, Diskus, Easibreathe, and pMDI. Majority of the COPD patients had clinically effective PIF on Turbohaler, and Autohaler. For the control group, none of the respondents had PIF below the clinically effective range. See table 2 for details of the distribution.

Table 2: PIF of COPD patients and control group across simulated internal resistance of DPI and pMDI

Variable	Frequency	Percentage	Frequency	Percentage
PIF	**Patients**		**Control**	
Clickhaler				
<15 l/min (suboptimal)	0	0.0	0	0.0
15-60 l/min (optimal)	75	100.0	75	100.0
Diskus				
<30 l/min (suboptimal)	0	0.0	0	0.0
30-90 l/min (optimal)	75	100.0	75	100.0
Turbohaler				
<30 l/min (suboptimal)	4	5.3	0	0.0
30-90 l/min (optimal)	71	94.7	75	100.0
Autohaler				
<30 l/min (suboptimal)	3	4	0	0.0
30-60 l/min (optimal)	72	96.0	75	100.0
Easibreathe				
<20 l/min (suboptimal)	0	0.0	0	0.0
20-60 l/min (optimal)	75	100.0	75	100.0
pMDI				
<25 l/min (suboptimal)	0	0.0	0	0.0
25-60 l/min (optimal)	75	100.0	75	100.0

PIF: Peak Inspiratory Flow
DPI: Dry powder Inhaler
pMDI: pressurized Metered Dose Inhaler

PIF across simulated internal resistance of DPI and pMDI stratified by the age range of COPD patients and control group

One-way ANOVA was used to determine the difference between the mean PIF across the age ranges of the COPD and control group. For the COPD group, there was no statistically significant difference in mean PIF between groups of age ranges across the simulated internal resistance of Clickhaler, Diskus, Turbohaler, Autohaler, Easibreathe and pMDI. However, there was an observed trend of a decrease in mean PIF as the age range increases (Table 3).

For the control group, there was no statistically significant difference in mean PIF between groups of age ranges for the Clickhaler internal resistance and pMDI. However, there was a statistically significant difference in mean PIF between groups of age ranges across the simulated internal resistance of Diskus ($F= 5.79$, $p= 0.001$), Turbohaler ($F= 5.80$, $p= 0.001$), Autohaler ($F= 7.41$, $p< 0.001$) and, Easibreathe ($F= 8.61$, $p< 0.001$) in the control group. There was also an observed trend of a decrease in mean PIF as the age range increases (Table 3).

Table 3: Comparing mean PIF across simulated internal resistance of DPI and pMDI stratified by age range of COPD patients and control group

Variable	Mean ± SD Patients	F	p-value	Mean ± SD Control	F	p-value
Age range	**Clickhaler**			**Clickhaler**		
50-59	50.83±9.56	0.65	0.583	57.71±5.71	0.47	0.701
60-69	49.40±11.42			59.00±15.86		
70-79	47.64±12.54			57.03±5.81		
80+	44.20±12.08			53.83±5.38		
	Diskus			**Diskus**		
50-59	64.00±13.62	0.98	0.409	66.86±13.02	5.79	0.001
60-69	60.67±14.34			62.41±15.44		
70-79	57.87±15.95			51.15±12.31		
80+	53.07±15.14			48.00±10.30		
	Turbohaler			**Turbohaler**		
50-59	50.83±10.13	1.47	0.231	55.29±10.55	5.80	0.001

60-69	46.47±13.33			51.91±9.11		
70-79	48.59±10.64			43.75±9.65		
80+	41.93±11.93			42.00±9.14		
	Autohaler			**Autohaler**		
50-59	65.33±26.88	1.75	0.164	73.57±14.26	7.41	0.000
60-69	60.67±17.55			67.23±15.85		
70-79	59.64±16.28			55.70±11.10		
80+	49.67±15.09			49.17±14.78		
	Easibreathe			**Easibreathe**		
50-59	75.65±22.39	2.47	0.069	90.71±18.71	8.61	0.000
60-69	74.47±19.19			80.77±17.20		
70-79	75.41±21.15			67.78±13.15		
80+	59.13±19.20			58.67±14.29		
	pMDI			**pMDI**		
50-59	82.83±8.45	1.78	0.158	113.14±8.86	2.03	0.117
60-69	91.13±21.14			106.05±15.63		
70-79	88.29±22.58			104.10±14.10		
80+	74.47±25.53			94.50±8.64		

F: One way ANOVA, pMDI: pressurized metered dose inhaler, DPI: dry powder inhaler, PIF: peak inspiratory flow

PIF across simulated internal resistance of DPIs and pMDI stratified by the sex of the study participants

Independent t-test was used to determine the difference between the mean PIF across the simulated internal resistance of DPI and pMDI stratified by the sex of the COPD group and control group. There was an observed trend of a greater mean PIF in males as compared to females among the study participants. For the COPD group, there was no statistically significant difference in mean PIF between the sex groups across the internal resistance of Clickhaler, Diskus, Autohaler, Easibreathe and pMDI. However, the mean PIF of the males was significantly greater than that of the females for Turbohaler (t=2.11, p=0.039). For the control group, there was no statistically significant difference in mean PIF between the sex groups across the simulated internal resistance of DPIs and pMDI (Table 4).

Table 4: Comparing mean PIF across simulated internal resistance of DPI and pMDI stratified sex of the patients and control group

Variable	Mean ± SD Patients	t	p-value	Mean ± SD Control	t	p-value
Sex	**Clickhaler**					
Male	49.55±12.10	1.74	0.087	56.23±5.21	-1.22	0.228
Female	44.74±11.37			59.00±13.67		
	Diskus					
Male	60.36±16.34	1.64	0.106	53.53±10.86	-1.49	0.140
Female	54.55±13.26			58.53±18.04		
	Turbohaler					
Male	49.32±11.29	2.11	**0.039***	46.05±8.55	-0.995	0.323
Female	43.74±11.29			48.47±12.52		
	Autohaler					
Male	60.20±16.57	1.12	0.267	58.09±11.28	-1.46	0.150
Female	55.61±18.78			63.09±18.38		
	Easibreathe					
Male	74.80±21.01	1.38	0.171	71.47±13.66	-0.89	0.374
Female	68.00±20.90			75.06±21.14		
	pMDI					
Male	89.82±21.80	1.94	0.057	106.91±12.32	1.54	0.127
Female	79.74±22.72			101.84±16.13		

pMDI: pressurized metered dose inhaler, DPI: dry powder inhaler, PIF: peak inspiratory flow, SD: Standard deviation

Correlation between age, anthropometric parameters and PIF of COPD patients

Pearson product moment correlation coefficient was used to analyse the relationship between age, anthropometric parameters and PIF of the patients. For Clickhaler, there was no significant correlation between PIF and age, weight, height and, BMI. For Diskus, there was a significant negative correlation between PIF and Age (r= -0.235, p= 0.043). For Turbohaler, there was a significant positive correlation between PIF and weight (r= 0.246, p= 0.034). For Autohaler, there was a significant negative correlation between PIF and age, weight as well as BMI. (Table 5)

Table 5: Correlation between age, anthropometric parameters (age, weight, height, BMI) and MI of COPD patients.

Variable		Age	Weight	Height	BMI
PIF Clickhaler	r-value p-value	-0.204 0.079	0.167 0.152	0.004 0.972	0.141 0.226
Diskus	r-value p-value	**-0.235*** **0.043**	0.216 0.063	0.100 0.395	0.143 0.222
Turbohaler	r-value p-value	-0.186 0.109	**0.246*** **0.034**	0.195 0.094	0.172 0.141
Autohaler	r-value p-value	**-0.258*** **0.025**	**0.294*** **0.010**	0.004 0.972	**0.264*** **0.022**
Easibreathe	r-value p-value	**-0.234*** **0.043**	**0.305**** **0.008**	0.084 0.473	0.223 0.055
pMDI	r-value p-value	-0.182 0.118	0.167 0.157	0.040 0.734	0.114 0.331

PIF- Peak inspiratory flow rate

r =Pearson correlation coefficient

** Correlation is significant at the 0.01 level

* Correlation is significant at the 0.05 level

Discussion

COPD is a growing global health concern, particularly in developing countries [3,15]. Dry powder inhalers (DPI) and pressurized metered dose inhalers (pMDI) play a crucial role in COPD inhalation therapy. While pMDIs use propellant or pressurized air as an energy source to generate fine particles, DPIs utilize the patient's peak inspiratory flow (PIF) as energy to break up the formulation in the DPI [16]. PIF significantly impacts total emitted dose (TED), fine particle fraction (FPF), and drug deposition in the airway. Due to variations in DPI design, their performance characteristics differ, influencing their suitability for diverse patient populations. PIFs depend not only on a patient's inhalation effort but also on the internal resistance of the device [17,18]. Therefore, resistance to airflow in DPIs is a key design parameter essential for optimizing inspiratory flow profiles and ensuring effective particle deposition in the airways [16]. This study explores PIF variations across different DPIs and examines the impact of age, gender and anthropometric parameters on PIF.

The control group had higher PIF than COPD group; however, only the clickhler and pMDI had statistically significant difference between the mean PIF of the patients compared with the control group. The reason for lower PIF in the COPD group may be secondary to respiratory muscle dysfunction in COPD which is multifactorial. It has been well established that the function of the diaphragm deteriorates in subjects with pulmonary emphysema. This is mainly due to pulmonary hyperinflation as a result of air trapping from airway obstruction [19]. Systemic factors like inflammation, oxidative stress, nutritional depletion, and the impact of specific drugs used in treatment can also influence respiratory muscle dysfunction [19]. Due to a combination these local and systemic factors, oxidative stress and epigenetic changes have been observed in the diaphragm and rib muscles of individuals with COPD [19].

In the COPD group, all study participants demonstrated clinically effective PIF with Clickhaler, Diskus, and Easibreathe. Although, the majority of patients with COPD achieved clinically effective PIF with Turbohaler and Autohaler, a minority were unable to achieve an optimal PIF of >30L/min. In contrast, none of the respondents in the control group had a PIF below the clinically effective range. Several studies have noted that certain DPIs, particularly Turbohaler, require a minimum PIF of 60 L/min for effective use [20-22]. However, a significant portion of our study participants did not reach the threshold of 60 L/min with the Turbohaler, with an average PIF recorded at 47 L/min. The PIFotal study revealed that 29% of COPD patients exhibited inspiratory flow lower than required for their DPI during their typical daily inhalation maneuvers. Furthermore, the study identified that suboptimal PIF and errors in inhalation technique were correlated with a diminished health status and poor adherence in individuals with COPD [23]. In another study, suboptimal PIF was associated with readmissions in patients with COPD [12]. These studies emphasize the significant negative impact of selecting an inhaler device that is not appropriately matched to the patient's PIF. Assessing device suitability is particularly important for some devices requiring higher PIF such as the Turbohaler. The turbohaler employs an integrated cyclone to disperse the formulation, establishing a higher inspiratory flow rate requirement for the effective aerosolization of drug particles. [7,24-26].

There was an observed trend of a decrease in mean PIF as the age range increases for the COPD group, with a significant negative correlation between PIF and age for Diskus, Autohaler and Easibreathe. Another study also demonstrated that, in elderly patients, the ability to generate adequate inspiratory flow across a

DPI is compromised, regardless of the presence of COPD [27]. Presence of impaired dexterity, cognitive decline, muscle weakness and, COPD severity are potential contributing factors for lower PIF among elderly patients [7,28,29]. The mean PIF of the males was greater than that of the females which was statistically significant for Turbohaler in our study participants with COPD. We also found a positive correlation between height and PIF although not statistically significant. Other studies also found that female gender and shorter height were associated with reduced PIF [29,30]. The variations in Peak Inspiratory Flow (PIF) between sexes may be attributed to the fact that women have smaller lung sizes than men, even when height-matched [31,32]. Additionally, women possess smaller large conducting airways and a shorter diaphragm, factors that could potentially influence pulmonary function [31,32]. However, some studies did not show any relationship between PIF and age, sex, or height [8].

In our study, 23% of the COPD patients were underweight. The COPD patients also had a statistically significant lower body weight and BMI than the controls. Also, increasing weight was associated with higher PIF with significant positive correlation between PIF and weight for Turbohaler, Autohaler and Easibreathe. PIF also increased with increasing BMI with significant positive correlation noted for Autohaler. Cachexia represents a distinct metabolic syndrome linked to a persistent underlying disease, such as COPD, marked by muscle wasting and weight loss [33]. Consistent findings from survival studies indicate notably higher mortality rates among underweight and normal-weight COPD patients compared to their overweight and obese counterparts [34,35]. The primary pillars for addressing muscle dysfunction in COPD involve rehabilitation-based exercises and enhanced nutrition. Pulmonary rehabilitation (PR) has proven to deliver physiological, symptom-alleviating, psychosocial, and health-economic advantages for individuals with chronic respiratory conditions, including COPD [33,36].

The importance of aligning the device with the individual's PIF cannot be overstated, as it directly influences the efficacy of the inhalation therapy and, consequently, the overall management of respiratory conditions including COPD. The consensus among most authors is that, when dealing with diminished inspiratory flow, a low-resistance DPI that shows relative insensitivity to airflow changes proves to be more advantageous [27]. Conversely, some authors documented that low-resistance DPIs may not be the best performers, as their regimen demands higher inspiratory airflow and effort, while medium-to-high-resistance inhalers (with the exception of turbohaler) require lower patient inspiratory flow rates for optimal performance [25,26]. In addition, some authors noted that the key factor influencing DPI performance is not the Peak Inspiratory Flow Rate but rather the negative pressure generated by the patient's inspiratory effort [37]. Regardless, it is of uttermost importance to ensure that devices are matched to patients' inspiratory effort.

Manufacturers should prioritize optimizing and controlling flow and dispersion characteristics in DPI formulations, possibly necessitating future designs where powder dose dispersion is independent of patient inhalation [38]. Additionally, they should be motivated to label products with specific resistance and the dose emitted at different flow rates to guarantee sufficient drug delivery [27]. In patients with suboptimal PIFs, active devices such as pMDIs or soft mist inhalers (SMIs) may be beneficial [7,25]. These devices (pMDIs and SMIs) are designed to be less dependent on the patient's inspiratory flow and may be suitable for individuals who struggle to generate high inspiratory flows, such as the elderly or those with respiratory muscle weakness [7,8]. Lastly, Healthcare providers should consistently assess and educate patients on the correct inhaler technique, as detailed in the GOLD 2023 report [4].

Conclusion

The observation that COPD patients tend to have slightly lower Peak PIF compared to controls is noteworthy. However, it is encouraging to note that despite this difference, most COPD patients using DPIs are still able to generate effective inspiratory flow rate requirement of 30l/min. This capability is crucial for ensuring adequate deposition of the drug in the lungs, thereby facilitating the therapeutic benefits of inhalation therapy.

It is important to consider factors such as increasing age, female sex, lower body weight and BMI, as they may contribute to lower PIF in COPD patients. This is particularly significant for devices requiring PIFs exceeding 60 L/min for optimal drug deposition. Understanding and addressing these variables are essential in optimizing inhalation therapy outcomes for individuals with COPD. Further research and individualized approaches may help tailor treatment strategies to accommodate the diverse characteristics and needs of COPD patients, ensuring the efficacy of inhalation therapy.

Limitations of this Study

As this is a cross-sectional study, establishing a cause-and-effect relationship cannot be reasonably determined. Our recommendations stem from clinical practice experience and warrant additional evaluation. The In-Check inspiratory meter only simulates the internal resistance of DPIs, so cut off for optimal versus suboptimal PIFs may not be precise. Other factors not assessed in this study may influence PIF measurement therefore, more studies are warranted.

Authors Contributions

All authors contributed to this work. Adebola Adetiloye: conceptualization, drafting, data analysis and interpretation, manuscript writing. Alexander Akor, Olayemi Awopeju: conceptualization, designing, and manuscript revising. Olufemi Adewole, Olurotimi Badero, Gregory Erhabor: data analysis and manuscript revising. All the authors have read and agreed to the final manuscript.

Conflict of Interest

The Authors declare that there is no conflict of interest.

Informed Consent

An informed consent given permission to us for using their data for searching purposes was obtained from all participants of the study.

Ethical Approval

Since the study exclusively utilized deidentified patient data already in existence, it was deemed exempt from ethical or institutional review board oversight or approval.

Data Availability

The data used to support the findings of this study are available at DOI. These prior studies are cited at relevant places within the text as references

Funding Statement

This research received no funding

References

[1] Buist AS, Vollmer WM, McBurnie MA. Worldwide burden of COPD in high- and low-income countries. Part I. The burden of obstructive lung disease (BOLD) initiative. Int J Tuberc Lung Dis. 2008;12(7):703-708. PMID: 18544191.

[2] Hurst JR, Skolnik N, Hansen GJ, et al. Understanding the impact of chronic obstructive pulmonary disease exacerbations on patient health and quality of life. Eur J Intern Med. 2020; 73:1-6. doi: 10.1016/J.EJIM.2019.12.014

[3] Chen S, Kuhn M, Prettner K, et al. The global economic burden of chronic obstructive pulmonary disease for 204 countries and territories in 2020: a health-augmented macroeconomic modelling study. Lancet Glob Health. 2023;11: e1183-e1193. doi:10.1016/S2214-109X (23)00217-6

[4] Terry PD, Dhand R. The 2023 GOLD Report: Updated Guidelines for Inhaled Pharmacological Therapy in Patients with Stable COPD. Pulm Ther. 2023;9(3):345. doi:10.1007/S41030-023-00233-Z

[5] Dhand PDTR. Inhalation Therapy for Stable COPD: 20 Years of GOLD Reports. Adv Ther. 2020;37(5): 1812-1828.doi: 10.6084/m9.figshare.11940423

[6] de Koning JP, van der Mark TW, Coenegracht PMJ, Tromp TFJ, Frijlink HW. Effect of an external resistance to airflow on the inspiratory flow curve. Int J Pharm. 2002;234(1-2):257-266. doi:10.1016/s0378-5173(01)00969-3

[7] Mahler DA. The role of inspiratory flow in selection and use of inhaled therapy for patients with chronic obstructive pulmonary disease. Respir Med. 2020; 161:105857. doi: 10.1016/J.RMED.2019.105857

[8] Ohar JA, Ferguson GT, Mahler DA, et al. Measuring Peak Inspiratory Flow in Patients with Chronic Obstructive Pulmonary Disease. Int J Chron Obstruct Pulmon Dis. 2022; 17:79. doi:10.2147/COPD.S319511

[9] Chrystyn H. Is inhalation rate important for a dry powder inhaler? Using the In-Check Dial to identify these rates. Respir Med. 2003;97(2):181-187. doi:10.1053/rmed.2003.1351

[10] Chew NYK, Chan HK. In vitro aerosol performance and dose uniformity between the Foradile® Aerolizer® and the Oxis® Turbuhaler®. Journal of Aerosol Medicine: Deposition, Clearance, and Effects in the Lung. 2001;14(4):495-501. doi:10.1089/08942680152744703

[11] Taylor A, Gustafsson P. Do all dry powder inhalers show the same pharmaceutical performance? Int J Clin Pract Suppl. 2005;59(149):7-12. doi:10.1111/J.1368-504X.2005. 00721.X

[12] Loh CH, Peters SP, Lovings TM, Ohar JA. Suboptimal Inspiratory Flow Rates Are Associated with Chronic Obstructive Pulmonary Disease and All-Cause Readmissions. Ann Am Thorac Soc. 2017;14(8):1305-1311. doi:10.1513/AnnalsATS.201611-903OC

[13] Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-68. doi:10.1183/09031936.05.00035205

[14] GOLD Spirometry Guide - Global Initiative for Chronic Obstructive Lung Disease - GOLD. Accessed November 30, 2023. https://goldcopd.org/gold-spirometry-guide/

[15] Boers E, Barrett M, Su JG, et al. Global Burden of Chronic Obstructive Pulmonary Disease Through 2050. JAMA Netw Open. 2023;6(12):2346598. doi:10.1001/jamanetworkopen.2023.46598

[16] Al-Showair RAM, Tarsin WY, Assi KH, Pearson SB, Chrystyn H. Can all patients with COPD use the correct inhalation flow with all inhalers and does training help? Respir Med. 2007;101(11):2395-2401. doi: 10.1016/J.RMED.2007.06.008

[17] Janssens W, VandenBrande P, Hardeman E, et al. Inspiratory flow rates at different levels of resistance in elderly COPD patients. Eur Respir J. 2008;31(1):78-83. doi:10.1183/09031936.

[18] Morén F. Aerosols in Medicine: Principles, Diagnosis, and Therapy. 1993. Amsterdam; New York: Elsevier

[19] Gea J, Pascual S, Casadevall C, Orozco-Levi M, Barreiro E. Muscle dysfunction in chronic obstructive pulmonary disease: update on causes and biological findings. J Thorac Dis. 2015;7(10): E418. doi: 10.3978/J.ISSN.2072-1439.2015.08.04

[20] Broeders MEAC, Molema J, Hop WCJ, Folgering HTM. Inhalation profiles in asthmatics and COPD patients: Reproducibility and effect of instruction. Journal of Aerosol Medicine: Deposition, Clearance, and Effects in the Lung. 2003;16(2):131-141. doi:10.1089/089426803321919898

[21] Mahler DA. Peak inspiratory flow rate as a criterion for dry powder inhaler use in chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2017;14(7):1103-1107. doi: 10.1513/AnnalsATS.201702-156PS

[22] De Boer AH, Gjaltema D, Hagedoorn P. Inhalation characteristics and their effects on in vitro drug delivery front dry powder inhalers Part 2: Effect of peak flow rate (PIFR) and inspiration time on the in vitro drug release from three different types of commercial dry powder inhalers. Int J Pharm. 1996;138(1):45-56. doi:10.1016/0378-5173(96)04526-7

[23] Leving MT, Bosnic-Anticevich S, van Cooten J, et al. Clinical recommendations for dry powder inhaler use in the management of COPD in primary care. NPJ Prim Care Respir Med. 2022; 32(1):1-8. doi:10.1038/s41533-022-00318-3

[24] Kondo T, Hibino M, Tanigaki T, Tajiri S, Horiuchi S. Optimal Inhalation Flow Pattern from Turbuhaler Predicted by Laser Photometry. J Aerosol Med Pulm Drug Deliv. 2022;35(3):139-145. doi: 10.1089/JAMP.2021.0001/ASSET/IMAGES/LARGE/JAMP.2021.0001_FIGURE6.JPEG

[25] Dal Negro RW. Dry powder inhalers and the right things to remember: a concept review. Multidiscip Respir Med. 2015;10(1). doi:10.1186/S40248-015-0012-5

[26] Levy ML, Carroll W, Izquierdo Alonso JL, Keller C, Lavorini F, Lehtimäki L. Understanding Dry Powder Inhalers: Key Technical and Patient Preference Attributes. Adv Ther. 2019;36(10):2547-2557. doi: 10.6084/m9.figshare.9577574

[27] Janssens W, VandenBrande P, Hardeman E, et al. Inspiratory flow rates at different levels of resistance in elderly COPD patients. European Respiratory Journal. 2008;31(1):78-83. doi:10.1183/09031936.00024807

[28] Adetiloye AO, Akor AA, Awopeju OF, Adewole OO, Adewuya OA, Erhabor GE. Effect of Chronic Obstructive Pulmonary Disease Severity on Inspiratory Flow Rates via

Inhaler Devices. West Afr J Med. 2023;40(9):989-996. PMID: 37768327.

[29] Mahler DA, Waterman LA, Gifford AH. Prevalence and COPD phenotype for a suboptimal peak inspiratory flow rate against the simulated resistance of the Diskus® dry powder inhaler. J Aerosol Med Pulm Drug Deliv. 2013;26(3):174-179. doi:10.1089/JAMP.2012.0987

[30] Ghosh S, Pleasants RA, Ohar JA, Donohue JF, Drummond MB. Prevalence and factors associated with suboptimal peak inspiratory flow rates in COPD. Int J Chron Obstruct Pulmon Dis. 2019; 14:585-595. doi:10.2147/COPD.S195438

[31] Molgat-Seon Y, Peters CM, Sheel AW. Sex-differences in the human respiratory system and their impact on resting pulmonary function and the integrative response to exercise. Curr Opin Physiol. 2018; 6:21-27. doi: 10.1016/J.COPHYS.2018.03.007

[32] Lomauro A, Aliverti A. Sex differences in respiratory function. Breathe. 2018;14(2):131. doi:10.1183/20734735.000318

[33] Jaitovich A, Barreiro E. Skeletal muscle dysfunction in chronic obstructive pulmonary disease what we know and can do for our patients. Am J Respir Crit Care Med. 2018;198(2):175-186. doi: 10.1164/RCCM.201710-2140CI/SUPPL_FILE/DISCLOSURES.PDF

[34] Kwan HY, Maddocks M, Nolan CM, et al. The prognostic significance of weight loss in chronic obstructive pulmonary disease-related cachexia: a prospective cohort study. J Cachexia Sarcopenia Muscle. 2019;10(6):1330-1338. doi:10.1002/JCSM.12463

[35] Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. Am J Clin Nutr. 2005;82(1):53-59. doi:10.1093/AJCN.82.1.53

[36] Rochester CL, Vogiatzis I, Holland AE, et al. An Official American Thoracic Society/European Respiratory Society Policy Statement: Enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation. Am J Respir Crit Care Med. 2015;192(11):1373-1386. doi:10.1164/RCCM.201510-1966ST

[37] Clark AR, Weers JG, Dhand R. The Confusing World of Dry Powder Inhalers: It Is All About Inspiratory Pressures, Not Inspiratory Flow Rates. J Aerosol Med Pulm Drug Deliv. 2020;33(1):1. doi:10.1089/JAMP.2019.1556

[38] Prime D, Atkins PJ, Slater A, Sumby B. Review of dry powder inhalers. Adv Drug Deliv Rev. 1997;26(1):51-58. doi:10.1016/S0169-409X (97)00510-3